

We Claim:

1. In a method to modulate exogenous gene expression comprising contacting an ecdysone receptor complex comprising:

- a) a DNA binding domain;
- b) a ligand binding domain;
- c) a transactivation domain; and
- d) a ligand;

with a DNA construct comprising:

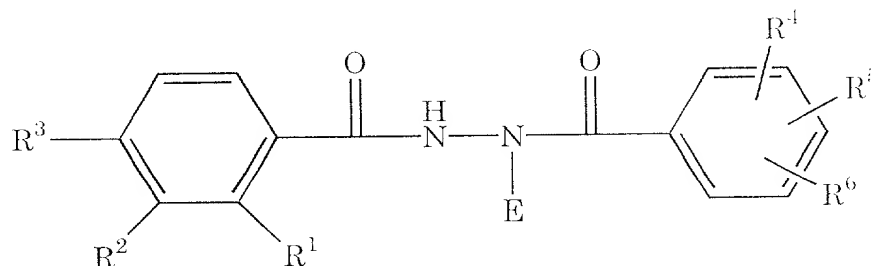
- a) the exogenous gene; and
- b) a response element;

wherein:

- a) the exogenous gene is under the control of the response element; and
- b) binding of the DNA binding domain to the response element in the presence of the ligand results in activation or suppression of the gene;

the improvement comprising:

selecting the ligand from a compound of the formula:



wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₁-C₅)alkyl

containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr,

SCN, SCHF_2 , SOMe , NH-CN , or joined with R^1 and the phenyl carbons to which R^2 and R^3 are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R^3 is H, Et, or joined with R^2 and the phenyl carbons to which R^2 and R^3 are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R^4 , R^5 , and R^6 are independently H, Me, Et, F, Cl, Br, formyl, CF_3 , CHF_2 , CHCl_2 , CH_2F , CH_2Cl , CH_2OH , CN, $\text{C}\equiv\text{CH}$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

a) when R^1 is Me and R^2 is OMe;

then R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

b) when R^1 is Me and R^2 is OEt;

then R^3 is H and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl ;

c) when R^1 is Et and R^2 is OMe or OEt;

then R^3 is H and the combination R^4 , R^5 , and R^6 is:

i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or

ii) R^6 is H, R^4 is Me, and R^5 is Et, F, Cl, Br, formyl, CF_3 , CHF_2 , CHCl_2 , CH_2F , CH_2Cl , CH_2OH , CN, $\text{C}\equiv\text{CH}$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

d) when R^1 is 1-Pr;

then R^2 is OMe, or OEt; R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;

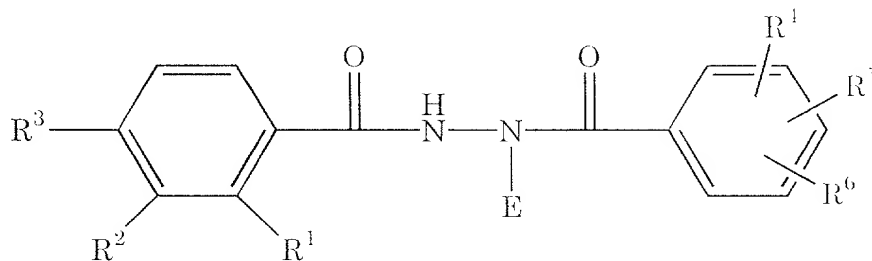
e) when R^3 is Et;

then R^2 is H, R^4 is F or Cl, and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;

- f) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;
then R^1 is Me or Et and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- g) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;
then R^1 is Et and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;
- h) when R^1 is formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN , $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OH , cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, SCN , or $SCHF_2$;
then R^2 is OMe or OEt , R^3 is H , and the combination R^4 , R^5 , and R^6 is 3,5-di-Me; and
- i) when R^2 is Me, Et, n-Pr, i-Pr, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN , $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH , O-n-Pr, OAc, NMe_2 , NEt_2 , SMe, SEt, $SOCF_3$, OCF_2CF_2H , COEt, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, OCF_3 , $OCHF_2$, O-i-Pr, SCN , $SCHF_2$, SMe, or $NH-CN$;
then R^1 is Et, R^3 is H , and the combination R^4 , R^5 , and R^6 is 3,5-di-Me.

2. A method to modulate exogenous gene expression comprising contacting an ecdysone receptor complex comprising:

- a) a DNA binding domain;
b) a ligand binding domain;
c) a transactivation domain; and
d) a ligand of the formula:



wherein:

E is a (C₁-C₆)alkyl containing a tertiary carbon or a cyano(C₁-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

a) when R¹ is Me and R² is OMe;

then R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

b) when R¹ is Me and R² is OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl ;

c) when R¹ is Et and R² is OMe or OEt;

then R³ is H and the combination R⁴, R⁵, and R⁶ is:

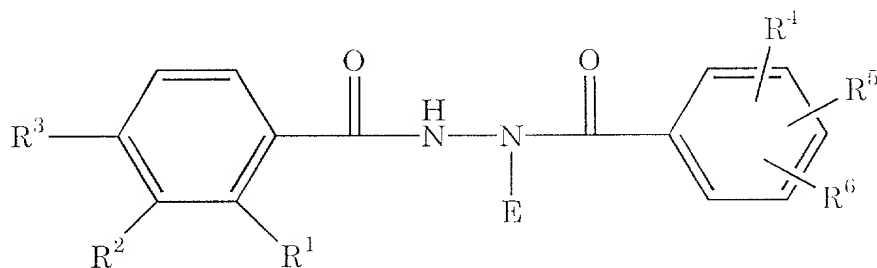
- i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
- ii) R^6 is H, R^4 is Me, and R^5 is Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;
- d) when R^1 is i-Pr;
then R^2 is OMe, or OEt; R^3 is H; and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;
- e) when R^3 is Et;
then R^2 is H, R^1 is F or Cl, and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;
- f) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;
then R^1 is Me or Et and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;
- g) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring,
then R^1 is Et and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;
- h) when R^1 is formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, SCN, or $SCHF_2$;
then R^2 is OMe or OEt, R^3 is H, and the combination R^1 , R^5 , and R^6 is 3,5-di-Me; and
- i) when R^2 is Me, Et, n-Pr, i-Pr, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe_2 , NEt_2 , SMe, SEt, $SOCF_3$, OCF_2CF_2H , COEt, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, OCF_3 , $OCHF_2$, O-i-Pr, SCN, $SCHF_2$, SMe, or NH-CN;
then R^1 is Et, R^3 is H, the combination R^1 , R^5 , and R^6 is 3,5-di-Me;
- with a DNA construct comprising:
- a) the exogenous gene; and
- b) a response element;

wherein:

- a) the exogenous gene is under the control of the response element; and
- b) binding of the DNA binding domain to the response element in the presence of the ligand results in activation or suppression of the gene.

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3. A method to modulate the expression of one or more exogenous genes in a subject, comprising administering to the subject an effective amount of a ligand of the formula:



wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₃-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the

oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R^1 , R^5 , and R^6 are independently H, Me, Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

a) when R^1 is Me and R^2 is OMe;

then R^3 is H; and the combination R^1 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

b) when R^1 is Me and R^2 is OEt;

then R^3 is H and the combination R^1 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl ;

c) when R^1 is Et and R^2 is OMe or OEt;

then R^3 is H and the combination R^1 , R^5 , and R^6 is:

i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or

ii) R^6 is H, R^4 is Me, and R^5 is Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

d) when R^1 is i-Pr;

then R^2 is OMe, or OEt; R^3 is H; and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;

e) when R^3 is Et;

then R^2 is H, R^1 is F or Cl, and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;

f) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;

then R^1 is Me or Et and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;

g) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;

then R^1 is Et and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;

h) when R¹ is formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

then R² is OMe or OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; and

i) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, or NH-CN;

then R¹ is Et, R³ is H, the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;

wherein the cells of the subject contain:

a) an ecdysone receptor complex comprising:

- 1) a DNA binding domain;
- 2) a binding domain for the ligand; and
- 3) a transactivation domain; and

b) a DNA construct comprising:

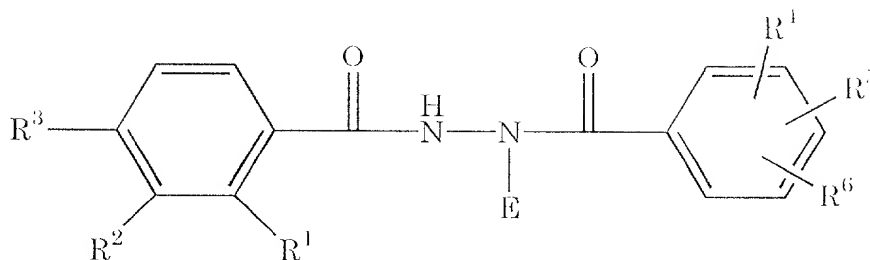
- 1) the exogenous gene; and
- 2) a response element; and

wherein:

- a) the exogenous gene is under the control of the response element; and
- b) binding of the DNA binding domain to the response element in the presence of the ligand results in activation or suppression of the gene.

4. A method for producing a polypeptide comprising the steps of:

- a) selecting a cell which is substantially insensitive to exposure to a ligand of the formula:



wherein:

E is a (C₁-C₆)alkyl containing a tertiary carbon or a cyano(C₁-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

a) when R¹ is Me and R² is OMe;

then R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

- b) when R^1 is Me and R^2 is OEt;
 then R^3 is H and the combination R^1 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl ;
- c) when R^1 is Et and R^2 is OMe or OEt;
 then R^3 is H and the combination R^1 , R^5 , and R^6 is:
 i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
 ii) R^6 is H, R^4 is Me, and R^5 is Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;
- d) when R^1 is i-Pr;
 then R^2 is OMe, or OEt; R^3 is H; and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;
- e) when R^3 is Et;
 then R^2 is H, R^1 is F or Cl, and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;
- f) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;
 then R^1 is Me or Et and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;
- g) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;
 then R^1 is Et and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;
- h) when R^1 is formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, SCN, or $SCHF_2$;
 then R^2 is OMe or OEt, R^3 is H, and the combination R^1 , R^5 , and R^6 is 3,5-di-Me; and
- i) when R^2 is Me, Et, n-Pr, i-Pr, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe_2 , NEt_2 , SMe, SEt, $SOCF_3$, OCF_2CF_2H ,

COEt, cyclopropyl, CF_2CF_3 , $\text{CH}=\text{CHCN}$, allyl, azido, OCF_3 , OCHF_2 , O-i-Pr, SCN, SCHF_2 , SOMe , or NH-CN ;

then R^1 is Et, R^3 is H, the combination R^1 , R^5 , and R^6 is 3,5-di-Me;

b) introducing into the cell:

1) a DNA construct comprising:

a) an exogenous gene encoding the polypeptide; and

b) a response element;

wherein the gene is under the control of the response element; and

2) an ecdysone receptor complex comprising:

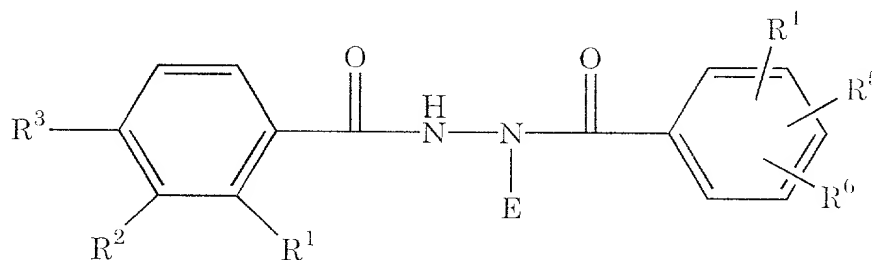
a) a DNA binding domain;

b) a binding domain for the ligand; and

c) a transactivation domain; and

c) exposing the cell to the ligand.

5. A method for regulating endogenous or heterologous gene expression in a transgenic organism comprising contacting a ligand of the formula:



wherein:

E is a $(\text{C}_4\text{-C}_6)$ alkyl containing a tertiary carbon or a cyano $(\text{C}_3\text{-C}_5)$ alkyl containing a tertiary carbon;

R^1 is H, Me, Et, i-Pr, F, formyl, CF_3 , CHF_2 , CHCl_2 , CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $\text{C}\equiv\text{CH}$, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF_2CF_3 , $\text{CH}=\text{CHCN}$, allyl, azido, SCN, or SCHF_2 ;

R^2 is H, Me, Et, n-Pr, i-Pr, formyl, CF_3 , CHF_2 , CHCl_2 , CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN, $\text{C}\equiv\text{CH}$, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe_2 , NEt_2 , SMe, SEt, SOCF_3 , $\text{OCF}_2\text{CF}_2\text{H}$, COEt, cyclopropyl, CF_2CF_3 , $\text{CH}=\text{CHCN}$, allyl, azido, OCF_3 , OCHF_2 , O-i-Pr, SCN, SCHF_2 , SOMe , NH-CN , or joined with R^3 and the

phenyl carbons to which R^2 and R^3 are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R^3 is H, Et, or joined with R^2 and the phenyl carbons to which R^2 and R^3 are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R^4 , R^5 , and R^6 are independently H, Me, Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

a) when R^1 is Me and R^2 is OMe;

then R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

b) when R^1 is Me and R^2 is OEt;

then R^3 is H and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl ;

c) when R^1 is Et and R^2 is OMe or OEt;

then R^3 is H and the combination R^4 , R^5 , and R^6 is:

i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or

ii) R^6 is H, R^4 is Me, and R^5 is Et, F, Cl, Br, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CN, $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

d) when R^1 is i-Pr;

then R^2 is OMe, or OEt; R^3 is H; and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;

e) when R^3 is Et;

then R^2 is H, R^1 is F or Cl, and the combination R^4 , R^5 , and R^6 is 3,5-di-Me;

f) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form an ethylenedioxy ring;

then R^1 is Me or Et and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;

g) when R^2 and R^3 , together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring;

then R^1 is Et and the combination R^1 , R^5 , and R^6 is 3,5-di-Me;

h) when R^1 is formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN , $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, SCN , or $SCHF_2$;

then R^2 is OMe or OEt, R^3 is H, and the combination R^1 , R^5 , and R^6 is 3,5-di-Me; and

i) when R^2 is Me, Et, n-Pr, i-Pr, formyl, CF_3 , CHF_2 , $CHCl_2$, CH_2F , CH_2Cl , CH_2OH , CH_2OMe , CH_2CN , CN , $C\equiv CH$, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe_2 , NEt_2 , SMe, SEt, $SOCF_3$, OCF_2CF_2H , COEt, cyclopropyl, CF_2CF_3 , $CH=CHCN$, allyl, azido, OCF_3 , $OCHF_2$, O-i-Pr, SCN , $SCHF_2$, SMe, or NH-CN;

then R^1 is Et, R^3 is H, the combination R^1 , R^5 , and R^6 is 3,5-di-Me;

with an ecdysone receptor complex within the cells of the organism wherein

the cells further contain a DNA binding sequence for the ecdysone

receptor complex when in combination with the ligand and wherein

formation of an ecdysone receptor complex-ligand-DNA binding sequence

complex induces expression of the gene.

6. The method of Claim 2 wherein the ligand is of the specified formula and E is t-butyl; R^1 is Me, Et, i-Pr, or F; R^2 is OH, OMe, OEt, or joined with R^3 and the phenyl carbons to which R^2 and R^3 are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R^4 is H, Et or joined with R^2 and the phenyl carbons to which R^2 and R^3 are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R^4 , R^5 , and R^6 are independently Me, F, Cl, CH_2OH , or OMe.

7. The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.
8. The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.
9. The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.
10. The method of Claim 2 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.
11. The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.

12. The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.
13. The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.
14. The method of Claim 2 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.
15. The method of Claim 3 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.
16. The method of Claim 4 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.
17. The method of Claim 5 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.
18. The method of Claim 3 wherein the subject is a plant
19. The method of Claim 3 wherein the subject is a mammal.